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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,613	07/18/2002	Oystein Rekdal	1181-258	3472

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EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,613	REKDAL ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8,9,11,13,20 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8,9,11,13,20 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on July 18, 2006. Claims 6, 8, 9, 11, 13, 20, and 24 are currently pending and are under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

3. Claim 6 is objected to because of the following informalities: the step of incorporating into the sector, which is opposite the cationic sector, has a grammatical error. The phrase describes a singular amino acid, 1 bulky and lipophilic amino acid[[s]]. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative

species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention.* Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

In the instant case, the claims are drawn to a method for the production of a pharmaceutical composition comprising mixing the peptide or a derivative thereof produced by the method of claim 6 with a pharmaceutically acceptable carrier.

(1) Level of skill and knowledge in the art:

The level of skill and knowledge in the art manufacturing peptide pharmaceuticals is high.

(2) Partial structure: / (3) Physical and/or chemical properties: / (4) Functional characteristics: / (5) Method of making the claimed invention:

The disclosure describes the method of producing a bioactive peptide, which is 7 to 25 amino acids in length, has at least 3 cationic amino acids and is capable of forming an amphipathic α-helix, which method comprises representing the peptide as a two-dimensional α-helical wheel identifying a cationic sector and dividing the remaining part of the peptide into three sectors substantially equal in size. Incorporating into the sector opposite the cationic sector

no more than 1 bulky and lipophilic amino acid, and incorporating into the combined two sectors flanking the cationic sector, two or more bulky and lipophilic amino acids, and synthesizing the peptide.

The disclosure describes the antibiotic and anti-tumor activity of amphipathic α-helical bioactive peptides. An alanine and lysine containing peptide comprising a bulky and lipophilic tryptophan amino acid residue in positions 7, 9, and 16 are shown to have cytotoxic activity in Meth A cells (see page 38, Table 1). Modified lactoferricin peptides are shown to have antibacterial activity against E. coli and S. aureus and reduced toxicity to red blood cells, and fibroblast cells (see page 39, Table 2).

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad genus. Claim 20 is a broadly generic to all possible **derivatives** of the bioactive peptides encompassed by the claims. The possible variations are enormous to any class of modifications. Since the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of modified bioactive peptides beyond those disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives of the bioactive peptide(s).

While having written description of peptides 7 to 25 amino acids in length having at least 3 cationic amino acids forming an amphipathic α-helical structure, and having no more than 1 bulky and lipophilic amino acid in the sector opposite the cationic sector identified in the specification tables and/or examples, the specification is devoid of any **derivatives thereof** that qualify for the functional characteristics claimed.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102/Claim Rejections - 35 USC § 103

6. Claims 6, 8, 9, 11, 13, 20, and 24 stand rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rekdal et al. (Journal of Peptide Science 5: 32-45 (Jan. 1999)).

The rejection was explained in the Office action mailed February 24, 2006.

Response to Arguments

7. Applicants' state Rekdal et al. do not anticipate or render obvious the presently claimed invention. Applicants' state the reference only distinguishes between a cationic and non-cationic

zone, while the present invention identifies four zones within the peptide of interest. The four sectors include a cationic sector, and three other sectors that are substantially equal in size as identified in an α-helical wheel representation. The claimed invention requires that at least 2 bulky and lipophilic amino acids should be incorporated into the sectors flanking the cationic sector and no more than 1 bulky and lipophilic amino acid can be in the sector opposite the cationic sector. Applicants' state the key features of the present invention are not taught or suggested in the cited reference.

Applicant's arguments filed July 18, 2006 have been fully considered but they are not persuasive. Rekdal et al. disclose the construction and synthesis of lactoferricin derivatives with enhanced antibacterial activity. Rekdal et al. states, "...the presence of an array of four basic residues on one face of the lactoferricins appeared to be important for antibacterial efficiency" (see page 38, 1st sentence in Design of Enhanced Peptides Based on the Bovine Lactoferricin Sequence section). Rekdal et al. do describe the synthesis of peptides with increases in both the lipophilicity and charge asymmetry that has significantly more activity against E. coli with a decreased minimum inhibitory concentration (see page 36, Table 2, and page 38, 7th sentence in Design of Enhanced Peptides Based on the Bovine Lactoferricin Sequence section). Rekdal et al. provides a helical wheel representations for LFB(17-31) F20, and LFB(17-31) K17, F20 peptides that are synthesized based on the description of enhanced antibacterial activity when there is an increase in lipophilicity and charge asymmetry. The peptides do have 4 sectors in a helical wheel representation, a cationic sector, the sector opposite the cationic sector having none or no more than 1 lipophilic amino acid, and the sectors adjacent to the cationic sector comprising at least 2 lipophilic and bulky amino acids. The cationic sector comprises 4 amino

acids, the sectors adjacent the cationic sector comprises more than 2 tryptophan amino acids (see Figure 4, C and D). The peptides are synthesized using solid phase synthesis techniques (see page 33, Synthesis of Peptides section). Therefore, Rekdal et al. do describe a method of synthesizing a bioactive peptide as is currently claimed.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

September 22, 2006

ROBERT A. WAX
PRIMARY EXAMINER